

Occupational exposure to respirable crystalline silica and risk of autoimmune rheumatic diseases, a nationwide cohort study

Supplementary material

Supplementary Table S1. Incidence rate ratios (IRR) of seropositive and seronegative rheumatoid arthritis following exposure to respirable crystalline silica among 1 541 505 men and 1 470 769 women, Denmark, 1979-2015

Exposure	Men						Women						
	Person-years	Seropositive			Seronegative			Person-years	Seropositive			Seronegative	
		Cases	IRR ^a (95 % CI)	Cases	IRR ^a (95 % CI)	Cases	IRR ^a (95 % CI)		Cases	IRR ^a (95 % CI)	Cases	IRR ^a (95 % CI)	
Cumulative exposure (µg/m³-years)													
0	28 567 899	1086	1	1357	1	30 865 519	3789	1	4657	1	4657	1	
2.0-29.2	1 579 301	101	1.31 (1.07-1.61)	108	1.16 (0.95-1.41)	341 276	45	0.82 (0.62-1.11)	64	0.98 (0.76-1.25)			
29.3-93.9	1 641 890	123	1.49 (1.24-1.80)	133	1.37 (1.15-1.64)	279 261	56	1.21 (0.93-1.58)	50	0.93 (0.70-1.22)			
94.0-1622	1 786 760	171	1.59 (1.35-1.88)	192	1.58 (1.36-1.85)	134 135	27	1.09 (0.75-1.59)	31	1.10 (0.77-1.57)			
<i>Per 50 µg/m³-years</i>			<i>1.08 (1.05-1.11)</i>		<i>1.07 (1.04-1.10)</i>				<i>1.05 (0.96-1.15)</i>			<i>1.03 (0.94-1.13)</i>	
<i>Per 50 µg/m³-years (exposed only)</i>			<i>1.03 (0.99-1.07)</i>		<i>1.02 (0.98-1.06)</i>				<i>1.06 (0.94-1.19)</i>			<i>1.06 (0.94-1.19)</i>	
Mean exposure (µg/m³)													
0	28 567 899	1086	1	1357	1	30 865 519	3789	1	4657	1	4657	1	
2.0-10.7	1 615 347	150	1.49 (1.26-1.77)	166	1.42 (1.21-1.67)	301 795	48	0.87 (0.65-1.15)	82	0.97 (0.76-1.24)			
10.8-18.0	1 656 775	133	1.51 (1.26-1.81)	133	1.28 (1.07-1.54)	267 145	47	1.09 (0.81-1.45)	47	1.09 (0.84-1.42)			
18.1-122.0	1 735 829	112	1.43 (1.17-1.73)	134	1.46 (1.22-1.75)	185 732	33	1.24 (0.88-1.75)	16	0.82 (0.56-1.22)			
<i>Per 50 µg/m³</i>			<i>2.51 (1.81-3.50)</i>		<i>2.40 (1.76-3.27)</i>				<i>1.32 (0.75-2.31)</i>			<i>1.00 (0.58-1.75)</i>	
<i>Per 50 µg/m³ (exposed only)</i>			<i>0.78 (0.38-1.59)</i>		<i>1.31 (0.68-2.53)</i>				<i>2.06 (0.64-6.66)</i>			<i>1.33 (0.40-4.47)</i>	
Highest attained exposure (µg/m³)													
0	28 567 899	1086	1	1357	1	30 865 519	3789	1	4657	1	4657	1	
2.0-12.0	1 584 153	135	1.48 (1.23-1.77)	141	1.30 (1.10-1.55)	334 045	50	0.84 (0.64-1.11)	76	1.06 (0.84-1.33)			
12.1-21.9	1 647 468	127	1.46 (1.21-1.75)	143	1.40 (1.18-1.66)	258 123	46	1.11 (0.83-1.49)	46	0.95 (0.71-1.28)			
22.0-122	1 776 330	133	1.50 (1.25-1.80)	149	1.47 (1.24-1.74)	162 504	32	1.31 (0.92-1.85)	23	0.83 (0.55-1.25)			
<i>Per 50 µg/m³</i>			<i>2.08 (1.63-2.66)</i>		<i>1.99 (1.58-2.51)</i>				<i>1.26 (0.77-2.07)</i>			<i>1.00 (0.62-1.63)</i>	
<i>Per 50 µg/m³ (exposed only)</i>			<i>1.10 (0.68-1.76)</i>		<i>1.36 (0.87-2.11)</i>				<i>1.71 (0.61-4.77)</i>			<i>1.23 (0.43-3.49)</i>	
Duration (years)													
0	28 567 899	1086	1	1357	1	30 865 519	3789	1	4657	1	4657	1	
1	975 669	49	1.14 (0.86-1.52)	53	1.01 (0.77-1.33)	210 968	29	0.92 (0.64-1.32)	39	1.03 (0.75-1.41)			
2-5	1 996 483	129	1.38 (1.15-1.66)	157	1.41 (1.19-1.66)	364 080	57	0.98 (0.75-1.27)	65	0.95 (0.74-1.21)			
6-39	2 035 799	217	1.66 (1.43-1.93)	223	1.51 (1.31-1.74)	179 624	42	1.18 (0.87-1.60)	41	1.00 (0.73-1.36)			
<i>Per year</i>			<i>1.03 (1.02-1.04)</i>		<i>1.03 (1.02-1.04)</i>				<i>1.01 (0.99-1.04)</i>			<i>1.00 (0.98-1.03)</i>	
<i>Per year (exposed only)</i>			<i>1.02 (1.00-1.03)</i>		<i>1.01 (0.99-1.02)</i>				<i>1.02 (0.98-1.06)</i>			<i>1.00 (0.96-1.04)</i>	

^a Adjusted for age (≤ 25 , 26-35, ≥ 36) and calendar year (1979-1985, 1986-1995, 1996-2005, 2006-2015)

Supplementary Table S2. Incidence risk ratio (IRR) of the studied autoimmune rheumatic diseases combined, systemic sclerosis, rheumatoid arthritis, systemic lupus erythematosus and small vessel vasculitis following exposure to respirable crystalline silica exposure among 1 541 505 Danish men when adjusting for probability of smoking, or adjusting for highest attained education or restricting analyses to 1 308 086 Danish men, working as blue collar workers at baseline

	The studied diseases combined ^a			Systemic sclerosis		Rheumatoid arthritis		Systemic lupus erythematosus		Small vessel vasculitis	
	Person-years ^b	cases	IRR (95 % CI)	cases	IRR (95 % CI)	cases	IRR (95 % CI)	cases	IRR (95 % CI)	cases	IRR (95 % CI)
<u>1 541 505 men, adjusted for age, calendar year and smoking probability^c</u>											
<u>Cumulative exposure (µg/m³-years)</u>											
0	28 527 938	3563	1	203	1	2630	1	198	1	587	1
2.0-29.2	1 576 698	283	1.15 (1.02-1.30)	8	0.63 (0.31-1.27)	218	1.15 (1.00-1.33)	18	1.41 (0.87-2.30)	46	1.27 (0.94-1.72)
29.3-93.9	1 639 692	351	1.31 (1.17-1.46)	14	0.94 (0.54-1.62)	267	1.31 (1.15-1.48)	16	1.19 (0.71-1.99)	57	1.45 (1.10-1.92)
94.0-1622	1 784 974	476	1.44 (1.31-1.59)	27	1.50 (0.99-2.26)	375	1.47 (1.32-1.64)	23	1.43 (0.92-2.22)	59	1.28 (0.98-1.69)
<i>Per 50 µg/m³-years</i>			<i>1.06 (1.05-1.08)</i>		<i>1.09 (1.01-1.17)</i>		<i>1.06 (1.04-1.08)</i>		<i>1.08 (1.00-1.17)</i>		<i>1.05 (1.00-1.10)</i>
<i>Per 50 µg/m³-years (exposed only)</i>			<i>1.04 (1.00-1.05)</i>		<i>1.11 (1.02-1.21)</i>		<i>1.02 (1.00-1.05)</i>		<i>1.07 (0.96-1.18)</i>		<i>0.99 (0.92-1.07)</i>
<u>1 541 505 men, adjusted for age, calendar year and education^d</u>											
<u>Cumulative exposure (µg/m³-years)</u>											
0	28 527 938	3563	1	203	1	2630	1	198	1	587	1
2.0-29.2	1 576 698	283	1.11 (0.98-1.25)	8	0.59 (0.29-1.20)	218	1.13 (0.98-1.30)	18	1.26 (0.78-2.06)	46	1.21 (0.89-1.64)
29.3-93.9	1 639 692	351	1.25 (1.12-1.40)	14	0.87 (0.50-1.50)	267	1.27 (1.11-1.44)	16	1.06 (0.63-1.77)	57	1.36 (1.03-1.80)
94.0-1622	1 784 974	476	1.37 (1.24-1.51)	27	1.37 (0.91-2.07)	375	1.40 (1.26-1.57)	23	1.31 (0.84-2.04)	59	1.23 (0.93-1.62)
<i>Per 50 µg/m³-years</i>			<i>1.06 (1.03-1.07)</i>		<i>1.08 (1.00-1.16)</i>		<i>1.06 (1.04-1.08)</i>		<i>1.07 (0.99-1.16)</i>		<i>1.04 (0.99-1.10)</i>
<i>Per 50 µg/m³-years (exposed only)</i>			<i>1.03 (1.01-1.06)</i>		<i>1.11 (1.02-1.22)</i>		<i>1.03 (1.00-1.05)</i>		<i>1.09 (0.98-1.20)</i>		<i>1.00 (0.93-1.08)</i>
<u>Restricted to 1 308 086 men working as blue collar worker at baseline^e</u>											
<u>Cumulative exposure (µg/m³-years)</u>											
0	25 519 083	3193	1	182	1	2348	1	183	1	525	1
2.0-29.2	1 500 720	271	1.25 (1.10-1.41)	8	0.73 (0.36-1.49)	208	1.26 (1.10-1.46)	17	1.39 (0.85-2.29)	44	1.35 (0.99-1.84)
29.3-93.9	1 591 052	340	1.41 (1.26-1.58)	14	1.08 (0.62-1.85)	258	1.42 (1.25-1.61)	16	1.23 (0.74-2.05)	55	1.50 (1.14-1.99)
94.0-1622	1 759 392	465	1.44 (1.30-1.59)	25	1.45 (0.94-2.22)	367	1.49 (1.33-1.67)	22	1.32 (0.84-2.08)	59	1.26 (0.95-1.65)
<i>Per 50 µg/m³-years</i>			<i>1.06 (1.04-1.08)</i>		<i>1.08 (0.01-1.16)</i>		<i>1.06 (1.04-1.08)</i>		<i>1.07 (0.99-1.15)</i>		<i>1.04 (0.99-1.09)</i>
<i>Per 50 µg/m³-years (exposed only)</i>			<i>1.01 (0.98-1.03)</i>		<i>1.09 (0.99-1.19)</i>		<i>1.01 (0.98-1.04)</i>		<i>1.04 (0.94-1.16)</i>		<i>0.97 (0.90-1.04)</i>

a The studied diseases combined: systemic sclerosis, rheumatoid arthritis, systemic lupus erythematosus, small vessel vasculitis

b Number of person-years used for each analysis of the different outcomes differed slightly. Only total person-years from the analysis of all autoimmune rheumatic disease are shown in the tables.

c Adjusted for age (≤ 25 , $26-35$, ≥ 36), calendar year (1979-1985, 1986-1995, 1996-2005, 2006-2015) and probability of smoking (5-25 %, 26-35 %, 36-74 %)

d Adjusted for age (≤ 25 , $26-35$, ≥ 36), calendar year (1979-1985, 1986-1995, 1996-2005, 2006-2015) and highest attained educational level (primary, secondary or vocational, short cycle higher, medium cycle higher, long cycle higher education or unknown.)

e Blue collar worker: ISCO 88 codes 6000-9999 at baseline, Adjusted for age (≤ 25 , $26-35$, ≥ 36) and calendar year (1979-1985, 1986-1995, 1996-2005, 2006-2015)

Supplementary Table S3. Distribution of person years and persons in each exposure group in the analysis of all diseases combined following exposure to respirable crystalline silica among 1 541 505 men and 1 470 769 women, Denmark, 1979-2015

	Men		Women	
	Person-years ^a	Persons ^b	Person-years ^a	Persons ^b
Cumulative exposure ($\mu\text{g}/\text{m}^3\text{-years}$)				
0	28 527 938	1 511 232	30 800 795	1 466 108
2.0-29.2	1 576 698	239 793	340 301	41 329
29.3-93.9	1 639 692	162 452	278 490	20 893
94.0-1622	1 784 974	82 156	133 920	6 409
Mean exposure ($\mu\text{g}/\text{m}^3$)				
0	28 527 938	1 511 232	30 800 795	1 466 108
2.0-10.7	1 612 428	155 618	300 872	26 902
10.8-18.0	1 654 722	104 483	266 425	14 629
18.1-122.0	1 734 214	72 950	185 414	7 470
Highest attained exposure ($\mu\text{g}/\text{m}^3$)				
0	28 527 938	1 511 232	30 800 795	1 466 108
2.0-12.0	1 581 211	144 199	333 072	27 537
12.1-21.9	1 645 575	76 090	257 420	10 509
22.0-122	1 774 578	57 937	162 219	5 250
Duration (years)				
0	28 527 938	1 511 232	30 800 795	1 466 108
1	974 370	266 325	210 515	42 914
2-5	1 993 555	216 932	363 012	31 650
6-39	2 003 439	121 317	179 184	12 700

^a Number of person-years for the analysis for of all studied diseases combined

^b Persons can contribute to more than one exposure group during the follow up period, hence number does not add up to the total study participants